**Title:**

# Evidence of both foetal inflammation and hypoxia-ischaemia is associated with meconium aspiration syndrome

**Short title: Foetal inflammation and meconium aspiration syndrome**

**Authors:**

**Kyoko Yokoi, M.D., Ph.D.[1], Osuke Iwata, M.D., Ph.D.[1], Satoru Kobayashi, M.D., Ph.D.[2], Mizuho Kobayashi, M.D.[3], Shinji Saitoh, M.D., Ph.D.[1], and Haruo Goto, M.D.[2]**

**Affiliations:**

**[1]Department of Pediatrics and Neonatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan**

**[2]Department of Pediatrics, Nagoya City University West Medical Centre, Nagoya, Japan**

**[3]Departments of Diagnostic Pathology, Nagoya City University West Medical Centre, Nagoya, Japan**

Supplementary Table S1: Multivariate logistic model including chorioamnionitis to explain the development of meconium aspiration syndrome (Model 2).

| | Odds ratio | | | |
|---|---|---|---|---|
| | | 95% Confidence interval | | P-value |
| | Mean | Lower | Upper | |
| Gestation (weeks) | 1.14 | 0.90 | 1.43 | 0.266 |
| Caesarean delivery | 1.50 | 0.90 | 2.51 | 0.123 |
| Female sex | 0.68 | 0.42 | 1.08 | 0.098 |
| Cord blood pH | 0.59 | 0.47 | 0.73 | <0.001 |
| Chorioamnionitis | 1.28 | 0.79 | 2.09 | 0.317 |
| $\alpha_1$-acid glycoprotein* | 1.02 | 1.01 | 1.04 | <0.001 |

**Notes:** Cord blood pH was calculated as per 0.10 pH change.
*Measured from umbilical cord or peripheral venous blood samples obtained approximately an hour after birth.

Supplementary Table S2: Multivariate logistic model including C-reactive protein to explain the development of meconium aspiration syndrome (Model 3).

| | Odds ratio | | | |
|---|---|---|---|---|
| | | 95% Confidence interval | | |
| | Mean | Lower | Upper | P-value |
| Gestation (weeks) | 1.11 | 0.88 | 1.40 | 0.380 |
| Caesarean delivery | 1.61 | 0.97 | 2.68 | 0.066 |
| Female sex | 0.68 | 0.43 | 1.09 | 0.106 |
| Cord blood pH | 0.58 | 0.47 | 0.73 | <0.001 |
| Funisitis | 2.92 | 1.71 | 5.01 | <0.001 |
| C-reactive protein* | 1.12 | 0.95 | 1.32 | 0.193 |

**Notes:** Cord blood pH was calculated as per 0.10 pH change.
*Measured from umbilical cord blood or peripheral venous blood samples obtained approximately an hour after birth.

Supplementary Table S3: Multivariate logistic model including the acute-phase inflammatory reaction score to explain the development of meconium aspiration syndrome (Model 4).

| | Odds ratio | | | |
|---|---|---|---|---|
| | | 95% Confidence interval | | P-value |
| | Mean | Lower | Upper | |
| Gestation (weeks) | 1.036 | 0.818 | 1.313 | 0.769 |
| Caesarean delivery | 1.473 | 0.879 | 2.468 | 0.141 |
| Female sex | 0.661 | 0.415 | 1.052 | 0.081 |
| Cord blood pH | 2.489 | 1.421 | 4.358 | 0.001 |
| Funisitis | 0.583 | 0.468 | 0.727 | <0.001 |
| Acute-phase inflammatory reaction score at birth* | | | | |
| 0 | Reference | | | |
| 1 | 1.971 | 1.139 | 3.411 | 0.015 |
| 2 or 3 | 2.171 | 1.137 | 4.146 | 0.019 |

**Notes:** Odds ratio for cord blood pH was calculated as per 0.10 pH change.
*Measured using cord blood or peripheral venous blood samples collected approximately one hour after birth. Acute-phase inflammatory scores of 0-3 were assigned according to the elevation of C-reactive protein, $\alpha_1$-acid glycoprotein, and haptoglobin (see Supplemental Material S1).

**Supplementary Information**

Supplemental Material S4: Acute-phase inflammatory response score

The acute-phase inflammatory response score is a composite score proposed as an early predictor of severe neonatal infection. Scores 0 (no positive biomarker), 1 (one positive biomarker), 2 (two positive biomarkers), and 3 (all three positive biomarkers) are defined according to the number of positive bed-side inflammatory biomarkers or C-reactive protein (>0.3 mg/dL), $\alpha_1$-acid glycoprotein (>20 mg/dL), and haptoglobin (>13 mg/dL). Score 3 assessed on day 0-1 is suggestive of severe neonatal infection requiring antibiotic therapies [32].